Health Canada Santé Canada

Your health and safety... our priority. *Votre santé et votre sécurité... notre priorité.*

Registration Decision RD2012-33

NeemAzal Technical, containing Azadirachtin

(publié aussi en français)

5 December 2012

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1925-0932 (print)
1925-0940 (online)

Catalogue number: H113-25/2012-33E (print version)
H113-25/2012-33E-PDF (PDF version)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2012

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

Registration Decision for NeemAzal Technical

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of NeemAzal Technical and TreeAzin Systemic Insecticide, containing the technical grade active ingredient azadirachtin, to control emerald ash borer and various insect pests that feed on the foliage of hardwood and softwood trees.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2012-16, *NeemAzal Technical, containing Azadirachtin*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for NeemAzal Technical and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2012-16.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2012-16, *NeemAzal Technical, containing Azadirachtin* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For

---

1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*"...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Azadirachtin?

Azadirachtin is the main component of a mixture of chemical compounds with insecticidal properties extracted from seeds of the tropical neem tree (*Azadirachta indica*). The precise mode of action is unknown; however, azadirachtin does affect insect hormones, interfering with moulting in immature insects and inhibiting reproduction in adult insects. Azadirachtin also has repellant properties, deterring insects from feeding and adult insects from laying eggs on treated plants. Formulated as TreeAzin Systemic Insecticide and injected into the trunks of host trees, it can provide control of emerald ash borer and of various insect pests that feed on the foliage of hardwood and softwood trees.

Health Considerations

Can Approved Uses of NeemAzal Technical Affect Human Health?

TreeAzin Systemic Insecticide, containing NeemAzal Technical, is unlikely to affect your health when used according to label directions.

Potential exposure to NeemAzal Technical may occur when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, NeemAzal Technical was of low acute toxicity via the oral and dermal routes of exposure. It was slightly toxic via the inhalation route, and therefore the hazard statement "CAUTION POISON" must appear on the label. NeemAzal Technical was not irritating to the skin, but was mildly irritating to the eyes, and caused an allergic skin reaction. Consequently, the hazard statements "CAUTION EYE IRRITANT" and "POTENTIAL SKIN SENSITIZER" are required on the label.

The end-use product TreeAzin Systemic Insecticide was of low acute toxicity to laboratory animals via the oral, dermal and inhalation routes of exposure. TreeAzin Systemic Insecticide was not irritating to skin, but was mildly irritating to the eyes. Consequently, the hazard statement "CAUTION EYE IRRITANT' is required on the label. It caused an allergic skin reaction, and as such, the hazard statement "POTENTIAL SKIN SENSITIZER" is required on the label.

The toxicology database for NeemAzal Technical did not contain the full array of studies normally required for pesticide registration. In the available studies there was no evidence to suggest that NeemAzal Technical damaged genetic material. Health effects in animals given repeated oral doses of NeemAzal Technical included effects on the blood, liver, thyroid and kidney. When NeemAzal Technical was given to pregnant animals, effects on the developing fetus (irregular bone ossification and heart abnormalities) were observed at a dose that also caused toxic effects in the mother, indicating that the young do not appear to be more sensitive to NeemAzal Technical than the adult animal. However, it is not possible to completely describe the potential human health effects of NeemAzal Technical due to the poor quality and limited nature of the available toxicology database. There is literature information reporting adverse reproductive effects in humans and other animals with other related neem compounds.

Exposure is expected to be low based on the fact that the product is injected directly into trees by licensed Pest Control Operators using a special delivery system. In addition, the use of an additional protective factor in the risk assessment serves to further reduce the allowable level of human exposure to NeemAzal Technical.

Residues in Water and Food

An analysis of the residues of azadirachtin in water and food was not required as there are no proposed food uses, and contamination of drinking water is not expected.

Risks in Residential and Other Non-Occupational Environments

Potential exposure and risks to bystanders are expected to be negligible if label directions and precautionary measures are followed.

For bystanders, the exposure is expected to be much less than for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Occupational Risks From Handling TreeAzin Systemic Insecticide

Occupational risks are not of concern when TreeAzin Systemic Insecticide is used according to the label directions, which include protective measures.

Commercial applicators who mix, load, or apply TreeAzin Systemic Insecticide using the EcoJect Tree Injection System can come in direct contact via skin and/or through inhalation exposure. Therefore, the label specifies that TreeAzin Systemic Insecticide must only be used with the EcoJect Tree Injection System and anyone mixing/loading and/or applying TreeAzin

Systemic Insecticide must wear long sleeved shirt and long pants, or coveralls over short sleeves and short pants, chemical-resistant gloves and goggles or a face shield during handling, loading, and application of product, and removal, clean-up, and repair of injection equipment. The label also specifies that entry to treated areas by bystanders is restricted until all insecticide is injected into the trees and the drilled holes are sealed. This ensures that there is no potential exposure to TreeAzin Systemic Insecticide from injection holes of host trees after application.

Taking into consideration these label statements, and the expectation of the exposure period for workers, the risks to these individuals are not a concern.

Environmental Considerations

What Happens When NeemAzal Technical Is Introduced Into the Environment?

NeemAzal Technical, containing the active ingredient azadirachtin, is injected into trees to control defoliating and burrowing insects. The risks to earthworms, birds, wild mammals, fish, terrestrial plants, amphibians, aquatic invertebrates, algae, or aquatic vascular plants from the use of azadirachtin as a tree injection is minimal. Risk to pollinators that may be exposed to residues in nectar and pollen from treated trees could, however, not be ruled out. To mitigate the potential risk to pollinators, precautionary and advisory label statements are required on the label and the treatment of hardwood tree species is restricted to the post-bloom period.

When NeemAzal Technical is injected into trees, azadirachtin is translocated from the trunk to other parts of the tree. The extent of translocation may be influenced by a variety of factors, including tree species, climatic conditions, and irrigation. Azadirachtin concentrations are highest in the leaves shortly after treatment and then gradually decline over time, primarily due to hydrolysis, such that the concentration in leaves of trees treated in spring and early summer are very low at leaf senescence.

Non-target organisms, such as birds, mammals and pollinators that feed on fruits, pollen or nectar of treated trees could be exposed to NeemAzal Technical. NeemAzal Technical is, however, not expected to pose a risk to birds and mammals. NeemAzal Technical is highly toxic to insect larvae and thus, has the potential to pose a risk to honeybees if the brood is exposed to contaminated pollen or nectar brought back to the hive by the adults. Similarly, NeemAzal Technical could pose a risk to other arthropods that feed on tree pollen and nectar of treated trees.

Non-target soil dwelling and aquatic invertebrates could also be exposed to NeemAzal Technical residues when the leaves of treated trees fall in autumn; however, because azadirachtin concentrations are low in leaves at senescence, a low environmental risk is expected from this exposure pathway. Biodegradation is expected to be important when the leaves of treated trees fall to soil or water.

Value Considerations

What Is the Value of TreeAzin Systemic Insecticide?

When injected into the trunks of host trees, TreeAzin Systemic Insecticide can provide control of emerald ash borer and various foliage-feeding insect pests.

TreeAzin Systemic Insecticide applied as an injection into the trunks of ash trees can provide control of emerald ash borer, a pest whose larvae bore under the bark of the trees, making them very difficult to control. If not controlled, emerald ash borer usually kills its host trees in North America, and to date the primary means of control has been to remove and destroy infested trees. Trunk injection of TreeAzin Systemic Insecticide can also substantially reduce damage to their respective host trees by a variety of foliage-feeding insect pests. TreeAzin Systemic Insecticide provides a new alternative active ingredient with a new mode of action for control of emerald ash borer and foliage-feeding pests of trees. Application by trunk injection helps conserve natural enemies of pests as well as other non-target organisms that would be exposed to foliar applications of insecticides.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of TreeAzin Systemic Insecticide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with TreeAzin Systemic Insecticide on the skin or through inhalation, anyone mixing, loading and/or applying TreeAzin Systemic Insecticide must: 1) wear a long sleeved shirt and long pants, or coveralls over short sleeves and short pants, chemical-resistant gloves and goggles or a face shield during handling, loading, and application of product and removal, clean-up and repair of injection equipment, 2) use only with the EcoJect Tree Injection System, and 3) restrict entry into treated areas until all insecticide is injected into the trees and the drilled holes are sealed.

Environment

TreeAzin Systemic Insecticide could pose a risk to pollinators. Label statements informing the users of the potential risks to these organisms are specified on the product label. Also, to reduce pollinator exposure, application to hardwood trees must be made post-bloom.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2012-16, *NeemAzal Technical, containing Azadirachtin* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, http://www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

---

[5] As per subsection 35(1) of the *Pest Control Products Act.*

Appendix I Comments and Responses

1. **A comment was received indicating that while the proliferation of emerald ash borer is a serious menace and the application of TreeAzin Systemic Insecticide is controlled and limited, doesn't justify Health Canada's registration of the product given the gaps in the toxicology database. In addition, the comment pointed out that the use is in urban environments and that the toxicity of the product to beneficial insects, such as bees, has been established.**

The PMRA has taken measures to minimise exposure to humans and the environment, including potential risk to pollinators. As a Commercial Class Product, occupational exposure is limited to licenced Pest Control Operators wearing the proper protective equipment. For residential exposure, the tree injection method minimises exposure to bystanders and the re-entry into treated areas is restricted until all of the insectide is injected into trees and the drilled holes are sealed. To address the gaps in the toxicology database, a 10 fold database uncertainty factor was applied as an added measure of protection and these gaps will have to be addressed for any future expansion of the use pattern involving NeemAzal Technical. Lastly, because a potential risk to pollinators was identified, precautionary and advisory label statements are required on the label and application to hardwood species is restricted to the postbloom period.

2. **A comment was received regarding the need for sealing of the injection site when protecting trees with TreeAzin Systemic Insecticide since trees have the ability to callus over small diameter holes within one growing season.**

The requirement to seal the injection site was placed on the label by the applicant, it was not based on an occupational exposure or environmental requirement. Nonetheless, it was used in the weight of evidence to justify the limited post-application exposure to human health.

3. **A comment was received on the need for label direction barring the product's use in greenhouses and requesting that the label should clearly specify the use outside of the bloom period due to its effect on bees.**

The PMRA generally does not include label statements specifying that a given product is not to be used in a greenhouse; rather, products that are registered for greenhouse use are clearly labeled as such. The label for TreeAzin Systemic Insecticide clearly indicates that the product is only for outdoor use on trees.

The label does include a statement that applications to hardwood trees must be made post-bloom, which is intended to minimise any potential adverse effects on bees.

4. **A comment was received on the welcome of registration of an additional product to combat emerald ash borer as the negative impacts of the infestation on forests have an impact on the quality of life of citizens.**

As part of Health Canada, the PMRA strives to protect the health and environment of Canadians while providing improved access to innovative pesticides for Canadians in an effective and transparent manner.